TRANSFORMING GROWTH FACTOR β (TGFβ) UNIQUELY REGULATES PRODUCTION AND STRUCTURE OF GLOMERULAR EXTRACELLULAR MATRIX PROTEOGLYCANS. W. Border, S. Okuda*, L. Languino*, E. Ruoslahti*. University of Utah Health Sciences Center, Salt Lake City, UT and La Jolla Cancer Research Foundation, La Jolla, CA.

Accumulation of extracellular matrix (ECM) is a prominent feature of progressive glomerulonephritis. Since some growth factors are known to stimulate ECM production we examined the effects of TGFβ, interleukin-1 (IL-1), platelet-derived growth factor (PDGF) and tumor necrosis factor (TNF) on the production of ECM by rat mesangial cells in culture. Cells were metabolically labeled with ^{35}S sulfate or ^{35}S methionine and conditioned media were analyzed by SDS-PAGE with fluorography combined with the use of enzymes or antibodies for specific molecular identification. In control experiments mesangial cells produced two species of proteoglycan identified as broad bands centered at 200 and 120 KD. These bands correspond in size to the small chondroitin/dermatan sulfate proteoglycans PG I and PG II (decorin) respectively; and, enzyme digestion showed both bands to be composed of chondroitin/dermatan sulfate. Exposure to TGFβ for 48 h greatly increased the PG I band and induced a structural change detected as a shift in electrophoretic mobility. TGFβ also produced a small increase in fibronectin but not laminin or type IV collagen. IL-1, PDGF or TNF had no substantial effects. These experiments show that TGFβ is unique among growth factors in its metabolic effects on glomerular ECM. The release of a substance like TGFβ in glomerulonephritis could stimulate the expansion of ECM and mediate the progression to glomerulosclerosis.

Exhibit C